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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,597	01/23/2004	Charles D. DeBoer	201448/351	7740

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EXAMINER	
THOMAS, DAVID C	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/763,597	DEBOER ET AL.	
	Examiner	Art Unit	
	David C. Thomas	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *28-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group 1, claims 1-27 and 32 in the reply filed on September 11, 2006 is acknowledged. Claims 28-31 are withdrawn from further prosecution. The traversal is on the grounds that the two inventions are closely related and that there is no burden searching both groups. This is not found persuasive for several reasons. First, the separate classification of the two groups is prima facie evidence of burden, which evidence has been rebutted. Second, the search for the methods of attaching nucleic acid molecules to electrically conductive surfaces of Group II is an entirely distinct search from the methods of detecting metallized target nucleic acid molecules, since the methods of attaching nucleic acid molecules to electrically conductive surfaces involves a search of references for attachment chemistry that is not required for the search of methods of detecting metallized target nucleic acid molecules.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1, 2, 4-8, and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by Gertner et al. (U.S. Patent Pub. No. 2003/0060873).

Gertner teaches a method for metallizing one or more sites of a nucleic acid molecule (for overview, see paragraph 11, lines 1-17 and paragraph 88, lines 10-14) comprising:

providing palladium ions (metal ions such as palladium are provided in a solution with bioactive materials, paragraph 12, lines 1-8 and paragraph 100, lines 10-13);

contacting the palladium ions and a nucleic acid molecule under conditions effective to bind the palladium ions on one or more sites of the nucleic acid molecule (palladium catalyst is deposited on surface of substrate such as DNA prior to electroless deposition, paragraph 45, lines 1-11, paragraph 62, lines 3-5, paragraph 100, lines 10-13, paragraph 88, lines 10-14 and Figure 5, step 40); and

contacting the nucleic acid molecule having palladium ions bound to one or more of its sites with nickel or nickel alloy under conditions effective to deposit nickel or nickel alloy on the nucleic acid molecule (after rinsing away palladium solution, substrate is ready for electroless deposition in aqueous solution containing nickel ions or a nickel alloy, paragraph 59, lines 1-8, paragraph 60, lines 1-7, paragraph 62, lines 1-8, and Figure 5, step 44).

With regard to claim 2, Gertner teaches a method wherein the nucleic acid molecule is DNA (bioactive materials that can be DNA such as genes, paragraph 27, lines 8-13 and paragraph 88, lines 10-14).

With regard to claim 4, Gertner teaches a method wherein the palladium ions are in an aqueous solution of palladium chloride (palladium catalyst is deposited on surface of substrate in form of solution of palladium chloride, paragraph 100, lines 9-14).

With regard to claims 5 and 7, Gertner teaches a method wherein said contacting the palladium ions and nickel or nickel alloy and a nucleic acid molecule is carried out for about 1 second to about 1 hour (after palladium catalyst is deposited on substrate, substrates were placed in electroless plating baths for 10 minutes, paragraph 102, lines 4-8).

With regard to claim 6, Gertner teaches a method wherein the nickel or nickel alloy is an electroless nickel plating solution (after rinsing away palladium solution, substrate is ready for electroless deposition or plating in aqueous solution containing nickel ions or a nickel alloy, paragraph 59, lines 1-8, paragraph 60, lines 1-7, paragraph 62, lines 1-8, and Figure 5, step 44).

With regard to claim 8, Gertner teaches a method further comprising:

washing away excess palladium ions from the nucleic acid molecule prior to said contacting the nucleic acid molecule having palladium ions bound to one or more of its sites with nickel or nickel alloy (surface of substrate is rinsed with distilled water to wash away palladium solution prior to electroless plating, paragraph 100, lines 10-15).

With regard to claim 26, Gertner teaches a method for metallizing one or more sites of a nucleic acid molecule comprising:

providing stannous ions (metals such as Sn (tin) can be used as sensitizing agents, paragraph 45, lines 3-7);

contacting the stannous ions and a nucleic acid molecule under conditions effective to bind stannous ions on one or more sites of the nucleic acid molecule

(substrate may be sensitized with stannous ions prior to performing electroless deposition process, paragraph 45, lines 3-7); and

contacting the nucleic acid molecule having stannous ions bound to one or more of its sites with silver under conditions effective to deposit silver on the nucleic acid molecule (substrate can also be catalyzed with silver prior to performing electroless deposition process, paragraph 45, lines 3-8 and paragraph 64, lines 1-8).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gertner et al. (U.S. Patent Pub. No. 2003/0060873) in view of Tu et al. (U.S. Patent No. 5,945,527).

Gertner teaches the limitations of claims 1, 2, and 4-8 as discussed above.

Gertner does not teach a method wherein the palladium ions are in a solution comprising palladium acetate, acetone, and water.

Tu teaches methods of modifying nucleosides or nucleic acids with bioagents using palladium-catalyzed reactions using palladium acetate in a solvent comprising water, ethyl acetate, and acetone (column 3, line 50 column 4, lines 15, column 8, lines 54-67, and claim 17).

Tu does not teach methods of metallizing one or more sites of a nucleic acid comprising contacting the nucleic acid molecule with nickel under conditions effective to deposit nickel or nickel alloy on the nucleic acid molecule.

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Gertner and Tu to modify nucleic acids by modifying bases on the nucleic acid with nickel or nickel alloys using the solution taught by Tu comprising a palladium catalyst, water, ethyl acetate, and acetone, along with a suitable nucleophile to attach to the nucleic acid. Thus, an ordinary practitioner would have been motivated to use such a solvent to modify the nucleic acids since the methods of Tu are versatile and can modify both pyrimidine and purine nucleosides at a variety of positions (Tu, column 1, lines 9-14 and claim 17), to produce labeled nucleic acids and oligonucleotides suitable for a variety of biological uses (Tu, column 1, lines 15-19 and column 4, lines 8-15).

7. Claims 9, 10, 12-25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fish (U.S. Patent Pub. No. 2004/0132220) in view of Gertner et al. (U.S. Patent Pub. No. 2003/0060873).

With regard to claims 9, 12, 16-19, and 26, Fish teaches a method for detecting a target nucleic acid molecule in a sample comprising:

providing a device for detecting the presence of a target nucleic acid molecule in a sample (for overview, see paragraph 15, lines 1-13) comprising:

two electrical conductors, including a first electrical conductor and a second electrical conductor, wherein the electrical conductors are not in contact with one another (two electrodes of opposite polarity are in close proximity but are prevented from direct contact, paragraph 17, lines 4-18 and paragraph 21, lines 19-26); and

one or more sets of two oligonucleotide probes attached to the electrical conductors, wherein the probes are positioned such that they cannot come into contact with one another (probes, or binding agents, are attached to surface of electrodes, paragraph 92, lines 11-13, paragraph 160, lines 1-4 and Figure 2C, parts 16 and 16a) and such that a target nucleic acid molecule, which has two sequences, a first sequence complementary to a first probe attached to the first electrical conductor and a second sequence complementary to a second probe attached to the second electrical conductor, can bind to both probes (two molecules of analyte, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to sequence on ends of nanotube, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D);

contacting the probes with a sample which may have the target nucleic acid molecule under selective hybridization conditions to permit target nucleic acid molecules (hybridization conditions are provided for optimal temperature and salt concentration, paragraph 161, lines 1-18), if any, present in the sample to hybridize to both of the probes and form a complex of the target nucleic acid molecule hybridized to the probes (two molecules of analyte, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to nanotube sequence, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D);

determining if an electrical current can be carried between the probes, said electrical current between the probes indicating the presence of the target nucleic acid molecule in the sample (presence of analyte places detection circuits of electrodes in second state to provide signaling and read-outs to indicate identity and/or amount of analyte present, paragraph 88, lines 1-12).

With regard to claim 10, Fish teaches a method wherein the target nucleic acid molecule is DNA or RNA (molecules that can be detected include DNA and RNA, paragraph 19, lines 1-13).

With regard to claim 13, Fish teaches a method wherein the sample is whole blood or peripheral blood lymphocytes (blood is removed directly from subject into the instrument, paragraph 114, lines 1-27; blood cells include T&NK cells, T helper cells, T cells, and suppressor cells, paragraph 168, lines 6-10).

With regard to claim 14, Fish teaches a method wherein said method is used to detect infectious agents (such as *E. coli* bacteria and other infectious agents, paragraph 14, lines 4-13, paragraph 114, lines 33-35 and paragraph 168, lines 10-11).

With regard to claim 15, Fish teaches a method wherein said method is used for nucleic acid sequencing (such as single-base sequencing for SNP applications, paragraph 159, lines 10-20).

With regard to claim 20, Fish teaches a method wherein the probes are complementary to sequences from the genetic material of a pathogenic bacteria (DNA of pathogens can be detected, paragraph 168, lines 1-11).

With regard to claim 21, Fish teaches a method wherein the pathogenic bacteria is a biowarfare agent (methods can be used for anti-terrorist pruposes, paragraph 14, lines 13-16).

With regard to claim 22, Fish teaches a method wherein the pathogenic bacteria is a food borne pathogen (method can be used for food and water safety measurements, paragraph 14, lines 13-15).

With regard to claim 23, Fish teaches a method wherein the probes are complementary to sequences from the genetic material of a virus (methods include assays for various viral agents such as HIV, hepatitis viruses, adenovirus, and influenza viruses, paragraph 157, lines 29-31).

With regard to claim 24, Fish teaches a method wherein the probes are complementary to sequences from the genetic material of a human (methods are used

in DNA diagnostics for human, as well as other animal and plant samples, paragraph 159, lines 20-25).

With regard to claim 25, Fish teaches a method wherein one or both of the probes has a sequence which is complementary to a sequence having a polymorphism, wherein the base or bases complementary to the polymorphism are located at an end of the probe distal to the conductors (method can be used to detect single nucleotide polymorphisms (SNPs), paragraph 159, lines 10-20; PCR or ligase chain reaction assays can be used for detecting specific sequences with the device, paragraph 162, lines 1-7).

With regard to claim 27, Fish teaches a method for detecting a target nucleic acid molecule in a sample comprising:

providing a device for detecting the presence of a target nucleic acid molecule in a sample (for overview, see paragraph 15, lines 1-13) comprising:

two electrical conductors, including a first electrical conductor and a second electrical conductor, wherein the electrical conductors are not in contact with one another (two electrodes of opposite polarity are in close proximity but are prevented from direct contact, paragraph 17, lines 4-18 and paragraph 21, lines 19-26); and

one or more sets of two oligonucleotide probes attached to the electrical conductors, wherein the probes are positioned such that they cannot come into contact with one another (probes, or binding agents, are attached to surface of electrodes, paragraph 92, lines 11-13, paragraph 160, lines 1-4 and Figure 2C, parts 16 and 16a) and such that a target nucleic acid molecule, which has two sequences, a first

sequence complementary to a first probe attached to the first electrical conductor and a second sequence complementary to a second probe attached to the second electrical conductor, can bind to both probes (two molecules of analyte, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to sequence on ends of nanotube, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D);

contacting the probes with a sample which may have the target nucleic acid molecule under selective hybridization conditions to permit target nucleic acid molecules (hybridization conditions are provided for optimal temperature and salt concentration, paragraph 161, lines 1-18), if any, present in the sample to hybridize to both of the probes and form a complex of the target nucleic acid molecule hybridized to the probes (two molecules of analyte, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to nanotube sequence, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D); and

determining if an electrical current can be carried between the probes, said electrical current between the probes indicating the presence of the target nucleic acid molecule in the sample (presence of analyte places detection circuits of electrodes in second state to provide signaling and read-outs to indicate identity and/or amount of analyte present, paragraph 88, lines 1-12).

Fish does not teach a method of providing palladium ions, such as in an aqueous solution of palladium chloride, and contacting the palladium ions with the device after said contacting the probes with the sample under conditions effective to bind the

palladium ions on one or more sites of any of the complex of the target nucleic acid molecules hybridized to the probes. Fish also does not teach a method of contacting the device with nickel or nickel alloy, wherein said contacting the device with nickel is carried out for about 1 second to about 1 hour, under conditions effective to deposit nickel or nickel alloy on the complex, after washing away excess palladium ions. Fish also does not teach a method of providing stannous ions, contacting the stannous ions with the device after said contacting the probes with the sample under conditions effective to bind the stannous ions on one or more sites of any of the complex of the target nucleic acid molecules hybridized to the probes, and contacting the device with silver under conditions effective to deposit silver on the complex of the nucleic acid molecules hybridized to the probes

Gertner teaches a method of providing palladium ions, such as in an aqueous solution of palladium chloride (palladium catalyst is deposited on the surface of a substrate in form of solution of palladium chloride, paragraph 100, lines 9-14), and contacting the palladium ions with a substrate after said contacting the probes with the sample under conditions effective to bind the palladium ions on one or more sites of any of the complex of the target nucleic acid molecules hybridized to the probes (after palladium catalyst is deposited on substrate, substrates were placed in electroless plating baths for 10 minutes, paragraph 102, lines 4-8). Gertner also teaches a method of contacting the device with nickel or nickel alloy under conditions effective to deposit nickel or nickel alloy on the complex after washing away excess palladium ions (after rinsing away palladium solution, substrate is ready for electroless deposition or plating

in aqueous solution containing nickel ions or a nickel alloy, paragraph 59, lines 1-8, paragraph 60, lines 1-7, paragraph 62, lines 1-8, and Figure 5, step 44). Gertner also teaches a method for metallizing one or more sites of a nucleic acid molecule comprising providing stannous ions (metals such as Sn (tin) can be used as sensitizing agents, paragraph 45, lines 3-7), contacting the stannous ions and a nucleic acid molecule under conditions effective to bind stannous ions on one or more sites of the nucleic acid molecule (substrate may be sensitized with stannous ions prior to performing electroless deposition process, paragraph 45, lines 3-7); and contacting the nucleic acid molecule having stannous ions bound to one or more of its sites with silver under conditions effective to deposit silver on the nucleic acid molecule (substrate can also be catalyzed with silver prior to performing electroless deposition process, paragraph 45, lines 3-8 and paragraph 64, lines 1-8).

Gertner does not teach a method of detecting a target nucleic acid molecule in a sample using a device comprising two electrical conductors wherein the conductors are not in contact with one another and each conductor has a probe attached such that a target molecule may hybridize to each probe.

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the methods of Fish for detecting a target molecule in a sample and Gertner for metallizing a nucleic acid such as a probe or target molecule since the methods of Gertner enable detection of the nucleic acid probe/target complex when the target is hybridized to two probes in the methods of the device taught by Fish. Thus, an ordinary practitioner would have been motivated to use

methods of using palladium or other metal catalysts to deposit metals or metal alloys such as nickel on nucleic acids using an electroless deposition method as taught by Gertner, since these methods provide an economical and scaleable approach to forming metal/bioactive structure complexes that do not damage the bioactive material in the process of deposition, since the conditions are mild, occurring at room temperature and near physiological pH, and are very controllable for a person of ordinary skill in the art (Gertner, paragraph 68, lines 5-22). Furthermore, the methods of Gertner are versatile, wherein a variety of catalysts such as palladium, tin and other metals can be used to sensitize the bioactive structure (Gertner, paragraph 45, lines 1-11) for deposition of a variety of metal particles such as nickel, silver, or gold (Gertner, paragraph 44, lines 1-10 and paragraph 64, lines 1-13).

8. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fish (U.S. Patent Pub. No. 2004/0132220) in view of Gertner et al. (U.S. Patent Pub. No. 2003/0060873) and further in view of Tu et al. (U.S. Patent No. 5,945,527).

Fish and Gertner teach the limitations of claims 9, 10, 12-25 and 27 as discussed above.

Fish and Gertner do not teach a method wherein the palladium ions are in a solution comprising palladium acetate, acetone, and water.

Tu teaches methods of modifying nucleosides or nucleic acids with bioagents using palladium-catalyzed reactions using palladium acetate in a solvent comprising water, ethyl acetate, and acetone (column 3, line 50 column 4, lines 15, column 8, lines 54-67, and claim 17).

Tu does not teach methods of metallizing one or more sites of a nucleic acid comprising contacting the nucleic acid molecule with nickel under conditions effective to deposit nickel or nickel alloy on the nucleic acid molecule. Tu also does not teach a method of detecting a target nucleic acid molecule in a sample using a device comprising two electrical conductors wherein the conductors are not in contact with one another and each conductor has a probe attached such that a target molecule may hybridize to each probe.

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the methods of Fish, Gertner, and Tu to modify nucleic acids by modifying bases on the nucleic acid with nickel or nickel alloys using the solution taught by Tu comprising a palladium catalyst, water, ethyl acetate, and acetone, along with a suitable nucleophile to attach to the nucleic acid. Thus, an ordinary practitioner would have been motivated to use such a solvent to modify the nucleic acids since the methods of Tu are versatile and can modify both pyrimidine and purine nucleosides at a variety of positions (Tu, column 1, lines 9-14 and claim 17), to produce labeled nucleic acids and oligonucleotides suitable for a variety of biological uses (Tu, column 1, lines 15-19 and column 4, lines 8-15). Such modified nucleic acids would be readily useable in the device of Fish since the modification occurs after the nucleic acid is bound to capture probes attached to the electrodes, and would thus not interfere with hybridization (Fish, Figure 2C and D).

9. Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fish (U.S. Patent Pub. No. 2004/0132220) in view of Zocchi et al. (U.S. Patent Pub. No. 2004/0241699).

With regard to claim 32, Fish teaches a method for detecting a target nucleic acid molecule in a sample comprising:

providing a device for detecting the presence of a target nucleic acid molecule in a sample comprising (for overview, see paragraph 15, lines 1-13):

two electrical conductors, including a first electrical conductor and a second electrical conductor, wherein the electrical conductors are not in contact with one another (two electrodes of opposite polarity are in close proximity but are prevented from direct contact, paragraph 17, lines 4-18 and paragraph 21, lines 19-26); and

one or more sets of two oligonucleotide probes attached to the electrical conductors, wherein the probes are positioned such that they cannot come into contact with one another (probes, or binding agents, are attached to surface of electrodes, paragraph 92, lines 11-13, paragraph 160, lines 1-4 and Figure 2C, parts 16 and 16a) and such that a target nucleic acid molecule, which has two sequences, a first sequence complementary to a first probe attached to the first electrical conductor and a second sequence complementary to a second probe attached to the second electrical conductor, can bind to both probes (two molecules of analyte, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to sequence on ends of nanotube, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D);

contacting the probes with a sample which may have the target nucleic acid molecule under selective hybridization conditions to permit target nucleic acid molecules (hybridization conditions are provided for optimal temperature and salt concentration, paragraph 161, lines 1-18), if any, present in the sample to hybridize to both of the probes and form a complex of the target nucleic acid molecule hybridized to the probes (two molecules of analyte in Figures 2C and D, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to nanotube sequence, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D);

attaching to the probes and any target nucleic acid molecule metal ions (such as electrically readable particles, which can include gold (paragraph 121, lines 1-17); and

determining the presence of the target nucleic acid molecule in the sample (presence of analyte places detection circuits of electrodes in second state to provide signaling and read-outs to indicate identity and/or amount of analyte present, paragraph 88, lines 1-12).

Fish does not teach a method of determining the presence of the target nucleic acid molecule in the sample by detecting the scatter of light caused by the metal ions attached to the probes and any target nucleic acid molecule.

Zocchi teaches a method of detecting polynucleotide hybridization using light scattering particles bound to the polynucleotide probe, including metal particles and colloidal metals such as colloidal gold (paragraph 41, lines 1-24).

Zocchi does not teach a method for detecting a target nucleic acid in a sample using a device comprising two electrical conductors wherein the conductors are not in contact with one another and each conductor has a probe attached such that a target molecule may hybridize to each probe.

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the methods of Fish for detecting a target molecule in a sample and Zocchi to detect polynucleotide hybridization since Zocchi teaches a highly sensitive method of detecting probe and target molecule hybridization using metal particles that scatter light to provide an alternative method for the detection system of Fish. Thus, an ordinary practitioner would have been motivated to use a light scattering detection system in the methods of Fish since this method is capable of detecting single target molecules with enhanced discrimination and eliminates the need to directly label the target, such as with fluorescent markers (Zocchi, paragraph 36, lines 1-19), thus providing a versatile assay and the means for more cost-effective devices (Zocchi, paragraph 35, lines 5-11). Furthermore, the methods of Zocchi is easily adaptable to the methods of Fish since probes can be linked to a solid surface such as a conductor or array matrix at one end and marked at the free end with a scatterer such as a metal particle (Zocchi, paragraph 41, lines 1-11).

Conclusion

10. Claims 1-27 and 32 are rejected. No claims are allowable.

Correspondence

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David C. Thomas whose telephone number is 571-272-3320. The examiner can normally be reached on 5 days, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David C. Thomas 9/22/06

David C. Thomas
Patent Examiner
Art Unit 1637

JEFFREY FREDMAN
PRIMARY EXAMINER
9/21/06